UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

August 18, 2017

MEMORANDUM:

Subject:	Name of Pesticide Product:	BAYOTHRIN TECHNICAL
	EPA Reg. No. /File Symbol:	432-RLII
	DP Barcode:	DP 435644
	Decision No.:	520689
	Action Code:	R060
	Submission:	#990378
	E-Sub.	13329
	PC Code:	129140 (Transfluthrin: 99%)

From: Byron T. Backus, Ph.D., Toxicologist
CITAB
Registration Division (7505P)

Byron T. Backus
August-18-2017

Through: P.V. Shah, Ph.D., Branch Chief
CITAB
Registration Division (7505P)

P.V. Shah
8/21/2017

To: Timothy Ciarlo, RM 03
IVB1
Registration Division (7505P)

Registrant: BAYER EMVIRPNMENTAL SCIENCE

FORMULATION FROM PROPOSED LABEL:

Active Ingredient(s):	by wt.
129140 Transfluthrin [CAS#118712-89-3].....	99.0%
Other Ingredients.....	1.0%
TOTAL	100.0%

ACTION REQUESTED: "...Please review the associated toxicology data and determine if they are acceptable to support registration of this new active ingredient. The proposed new AI is transfluthrin, a pyrethroid class insecticide intended for indoor and limited outdoor control of mosquitoes and other flying insect pests. The registrant has an agreement with a third party company, which is concurrently submitting an application for a new end-use product containing transfluthrin... A separate bean will be created for that action. I have included the following:

1. Cover letter and transmittal document both dated 6/30/2016
2. Data matrix dated 7/27/2016
3. Proposed label
4. Basic CSF dated 7/11/2016

MRIDs are available in Documentum..."

BACKGROUND: The acute toxicity studies are in MRIDs 49617850 (oral LD_{50}); 49617851 (dermal LD_{50}); 49617852 (inhalation LC_{50}); 49617853 (dermal and eye irritation); and 49617854 (dermal sensitization).

COMMENTS AND RECOMMENDATIONS:

1. CITAB has reviewed the six acute toxicity studies in MRIDs 496178-50 through -54.

2. The dermal sensitization study (MRID 49617854) has been classified as supplementary, because the report does not include a positive control study conducted within 6 months of the study with NAK 4455. The classification of this study can be upgraded with a positive control study conducted within six months of the report date.

3. The remaining studies have been classified as acceptable.

4. In the acute inhalation study (MRID 49617852) rats were exposed for 4 hours to 0.5126 mg NAK 4455/L with no mortality, indicating an inhalation $LC_{50} > 0.5126$ mg/L, with assignment to toxicity category III by the inhalation exposure route.

5. In the eye irritation study (MRID 49617853) the test material is described as a liquid. However, the test material can also be a solid at normal temperatures (from p. 10 of MRID 49617808 the technical (99.1%) is described as off-white needles; from p. 8 of MRID 49617817: "The test item has a melting point at atmospheric pressure of 32° C"). While the results from MRID 49617854 would normally result in a toxicity category IV classification for eye irritation potential, there is a possibility that exposure to the crystalline form could be more irritating. As a result (and in the absence of testing with the crystalline form) technical transfluthrin has been assigned to toxicity category III for eye irritation.

6. Based on the results from the six acute toxicity studies, the following is the acute toxicity profile for 432-RLII:

Oral LD_{50} (rat)	Toxicity Category IV	MRID 49617850	Acceptable
Dermal LD_{50} (rat)	Toxicity Category IV	MRID 49617851	Acceptable
Inhalation LC_{50} (rat)	Toxicity Category III	MRID 49617852	Acceptable
Eye Irritation (rabbit)	Toxicity Category III	MRID 49617853	Acceptable
Dermal Irritation (rabbit)	Toxicity Category IV	MRID 49617853	Acceptable
Dermal sensitization (g. pig)	Negative	MRID 49617854	Supplementary*

*The study can be upgraded with an acceptable positive control assay conducted at the same test facility within six months of the report date.

7. Based on the acute toxicity profile above, the following is the precautionary and first aid labeling for Bayothrin Technical (99% Transfluthrin) as obtained from the Label Review System:

PRODUCT ID #: **000432-01588**

PRODUCT NAME: **BAYOTHRIN TECHNICAL**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: **CAUTION**

Hazards to Humans and Domestic Animals:

Harmful if inhaled. Causes moderate eye irritation. Avoid breathing spray mist. Remove and wash contaminated clothing before reuse. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Wear: Long-sleeved shirt and long pants, Socks, and Shoes.

First Aid:

If inhaled:
-Move the person to fresh air.
-If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
-Call a poison control center or doctor for further treatment advice.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

8. All acute toxicity study requirements for the registration of 432-RLII will be satisfied when the Agency has an acceptable dermal sensitization study on file (either through an upgrade of the study in MRID 49617854 or a new study has been received and classified as acceptable).

Reviewer: Byron T. Backus, Ph.D.
Date: August 18, 2017
Risk Manager (EPA): 03

The following is the Acute Toxicity Data Evaluation Record (DER) for the acute toxicity studies (MRIDs 496178-50 through -54) submitted to support the registration of EPA File Symbol 432-RLII (Bayothrin Technical).

2. PC CODE: 129140 (Transfluthrin 99%)

3. CURRENT DATE: August 18, 2017

4. TEST MATERIAL: From p. 12 of MRID 49617850: NAK 4455 technical active ingredient; batch no. 130187, purity 94.5%; described as a dark brown solid/liquid (melting point: 50° C, pH 4.4 (2% in water). For the inhalation study (see p. 11 of MRID 49617852) batch number was 250 987 and purity was 97.5% (from p. 63 of MRID 49617852 purity was 94.5%). The dermal sensitization study used the same batch but reported (p. 12 of MRID 4961784) 95.0% purity. For the dermal and eye irritation studies the batch number was NAK 4455-III-4733, described (p. 11 of MRID 49617853) as a colorless liquid containing 95% active ingredient. From p. 10 of MRID 49617808 technical (99.1%) is described as off-white needles; from p. 8 of MRID 49617817: "The test item has a melting point at atmospheric pressure of 32° C."

Study	MRID	Results	Tox Cat	Core Grade
Acute oral toxicity / rat / Bayer AG Fachbereich Toxikologie (Toxicology Division), Wuppertal 1, Germany / Report No. 17160; Study No. T 4025025 / 14 September 1988 / OCSPP 870.1100; OECD 401	49617850	Groups of 5M & 5F fasted Bor: WISW(SPF-Cpb) Wistar rats were dosed (by stomach tube) at 100, 1000, 2500 and 5000 mg NAK 4455/kg. For dosing, NAK 4455 was dissolved in polyethylene glycol; dosing volumes were either 5 or 10 mL/kg. Results: One 5000 mg/kg female died on day 1; all other rats survived. No toxicity at 100 mg/kg. At 1000 mg/kg there was apathy, tremor, bristling coat and (females only) spasmodic posture, with recovery by day 6. At 2500 signs also included spasmodic tremor with recovery by day 6. At 5000 mg/kg signs included those seen at 2500 mg/kg plus accelerated respiration and (females only) spastic gait and moist anus, with recovery by day 8. No effects on bodyweights of 3 lowest doses; 5000 mg/kg group rats had reduced (~10 to ~20 g) body weight gains relative to other groups. Gross necropsy of the dead female showed slightly patchy and slightly distended lung, patchy kidneys, and very reddened glandular stomach. There were no gross findings in other rats. Oral LD_{50} > 5000 mg/kg.	IV	A

Acute dermal toxicity / rat / Bayer AG Fachbereich Toxikologie (Toxicology Division), Wuppertal 1, Germany / Report No. 17155; Study No. T 5025026 / 14 September 1988 / OCSPP 870.1200; OECD 402	49617851	Groups of 5M & 5F Bor: WISW (SPF-Cpb) Wistar rats received 24-hr occluded exposure to 100, 1000, 2500 or 5000 mg NAK 4455/kg. "The test compound was mixed to a paste before application with four per cent by weight cellulose powder for better adhesion to the skin." Results: There was no mortality. There were no signs of toxicity at 100 mg/kg. At 1000 and 2500 mg/kg rats showed apathy and (females only) vocalization, with recovery by day 2. At 5000 mg/kg there was apathy, spasmodic posture, weak tremor and (females only) vocalization, with recovery by day 4. Mean body weight gains were similar for all groups by sex. There were no gross findings at necropsy. Dermal LD_{50} > 5000 mg/kg.	IV	A
Acute inhalation toxicity / rat / Bayer AG Toxicology Department, Wuppertal 1, Germany / Report No. 17216; Study No. T5029572 / 14 October 1988 / OCSPP 870.1300; OECD 403	49617852	5M & 5F Bor: WIS (SPF-Cpb) Wistar rats were exposed (nose only) for 4 hrs to a mean concentration of 512.6 mg NAK 4455/m^3 (=0.5126 mg NAK 4455/L) aerosolized ("nebulized") as a 25% dilution in 50% polyethylene glycol E 400 and 50% ethanol. MMAD = 1.44 µm; mean GSD = 1.42. The mass fraction (%<5 µm) was 100%. Results: There was no mortality. Male rats had no signs of toxicity; all females had slight transient (~5 minutes) tremor immediately after exposure, but otherwise had no signs. Reflex tests (corneal, primal, myotonic, light, righting, startle) showed no exposure-related effects. Gross necropsy (after 14-day observation) showed no macroscopically visible lung or other organ damage. A control group of 10M and 10F was similarly exposed to vehicle alone, with no mortality or signs of toxicity. There were no significant differences between the control and NAK 4455-exposed groups with respect to weight gains. Inhalation LC_{50} (both sexes) > 0.5126 mg NAK 4455/L.	III	A

Primary eye irritation / rabbit / Bayer AG Fachbereich Toxikologie Wuppertal-Eberfeld, Germany / Report No. 15804; Study No. T 5023406 / 20 May 1987 / OCSPP 870.2400; OECD 405	49617853	100 µL (=0.1 mL) was instilled in the conjunctival sac of one eye of each of 3 NZW rabbits. The lids were held together for about one second. The treated eye was washed out with physiological saline at 24 hours, with Draize scoring at 1, 24, 48 and 72 hrs and on day 7. Results: No corneal opacity or iritis at any time. At 1 hr all 3 eyes scored 1 for redness, 2-3 for chemosis, and 1-3 for dacryorrhea (described in the report as tear flow and/or discharge). At 24 hrs one eye scored 1 for chemosis; all other scores were zero. All scores were zero at 48 and 72 hrs, and on day 7. The Maximum Mean Eye Irritation Score = 10.67 (at 1 hr). Normally assignment would be to toxicity category IV. However, on p. 10 of MRID 49617808 technical (99.1%) is described as off-white needles. From p. 8 of MRID 49617817: "The test item has a melting point at atmospheric pressure of 32° C." Since the test material can be in the form of [crystalline?] needles (with possibility of mechanical irritation) at room temperature, technical transfluthrin is assigned to toxicity category III for eye irritation.	III	A
Primary dermal irritation / rabbit / Bayer AG Fachbereich Toxikologie Wuppertal-Eberfeld, Germany / Report No. 15804; Study No. T 5023406 / 20 May 1987 / OCSPP 870.2500; OECD 404	49617853	The study used 3 NZW rabbits. For each of these rabbits, 500 µL (=0.5 mL) was applied to a dressing which in turn was applied to a skin area of about 6 cm^2 with 4 hours of semiocclusive exposure. Application sites were scored (Draize) at 1, 24, 48 and 72 hrs and at 7 days. Results: all dermal irritation scores (for both erythema and edema) were zero. PDII = 0.00	IV	A

Dermal sensitization: Buehler Test / guinea pig / Bayer AG Toxicology Department, Wuppertal 1, Germany / Report No. 17920; Study No. T6029915 / 14 April 1989 / OCSPP 870.2600; OECD 406	49617854	12 male guinea pigs were each dermally treated (6-hr exposures) on the left flank with 0.5 mL undiluted NAK 4455 technical three times, with 7-day intervals between exposures. From p. 16 of MRID 49617854: "After lengthy cooling the test compound had the form of a solid mass at room temperature. For administration the substance was melted at 50° C, and remained liquid even after short cooling." Two weeks after the third exposure the guinea pigs were challenged (on the left flank) with 0.5 mL undiluted NAK 4455; a control (previously unexposed) group of 12 guinea pigs was similarly treated. Sites were scored at 24, 48 and 72 hours after challenge. Results: All scores following challenge in both the previously exposed and control guinea pigs were zero. There was no indication that the test material is a sensitizer. MRID 49617854 is currently classified as supplementary because it does not include a positive control study conducted within 6 months of the study with NAK 4455. The study can be upgraded with an acceptable positive control assay conducted at the same test facility within six months of the report date.	(Negative)	S (no positive control)

n.d. = not determined; Core Grade Key: A =Acceptable, S = Supplementary, W = Waived, U = Unacceptable, D = Data Gap